University, Chicago, IL; [3] Hematology/Oncology, Northwestern University Feinberg School of Medicine, Chicago, IL

Introduction: Pain following hematopoietic stem cell transplantation (HSCT) is caused by several factors: chemotherapy, radiotherapy, infections, GVHD, and medications. Difficulties in defining and accurately diagnosing pain symptoms can lead to delays in starting effective analgesia and poorer quality of life. Pain syndromes following HSCT have not been well-studied and the actual prevalence is unknown. The goal of this study was to determine incidence, severity, and the time course of pain following HSCT.

Method: We designed a prospective, observational study which enrolled 100 patients undergoing HSCT (60% autologous, 40% allogeneic. 19 unrelated, 13 sibling, 8 double cord. Myeloma 44%, leukemia 29%, lymphomas 26%, and aplastic anemia 1%). Patients enrolling on the study completed 5 questionnaires before HSCT and 1, 2, 3, 6, 9, and 12 months after HSCT. The questionnaires were the Brief Pain Inventory (BPI), the EORTC Quality of Life Questionnaire-Chemotherapy Induced Peripheral Neuropathy (EORTC-CIPN), the Muscle and Joint Measure (MJM), the MD Anderson Symptom Index – Graft-versus-Host Disease module (MDASI-cGVHD), and the Hospital Anxiety and Depression Scale (HADS).

Results: At the 9-month review, we found that there was a significant increase in pain reported after allogeneic HSCT compared to pre-HSCT. (71% increase at 3 months; p=0.01). This difference was independent of conditioning regimen, disease or GVHD. For autologous HSCT, there was an increase in reported neuropathic symptoms (47% increase at 3 months; p=0.02). We also found and increase in muscle cramping and spasms late after HSCT; both autologous and allogeneic (99% increase at 9 months; p=0.03). Muscle cramping interfered with sitting, standing and physical activity (21% at 6 months; p=0.04 and 136% at 9 months; p=0.04). The increase in muscle cramping symptoms was independent of conditioning regimen, disease or GVHD.

Conclusions: Our current review of this study reveals that pain and muscle cramping is a significant symptom that develops after both allogeneic and autologous HSCT. This appears to be independent of conditioning regimen, disease or GVHD.

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Management of Catheter-Related Thrombosis in Patients Undergoing Autologous Stem Cell Transplantation

*Manish Sharma [1], **Mahasweta Gooptu [2]**, Thomas Klumpp [2], Neeraj Saini [3], Ashok Mandala [3], Sherilyn Tuazon [3], Srikanth Nagalla [4], John Wagner [3], Margaret Kasner [3], Onder Alpdogan [3], Ubaldo Martinez [5], Dolores Grosso [3], Joanne Filicko [6], Barbara Pro [3], Matthew Carabasi [3], Neal Flomenberg [3], Mark Weiss [3]. [1] Medical Oncology, Thomas Jefferson University, Philadelphia, PA; [2] Medical Oncology, Thomas Jefferson University Hospital, Philadelphia, PA; [3] Medical Oncology, Thomas Jefferson University, Philadelphia, PA; [4] Thomas Jefferson University, Philadelphia, PA; [5] Department of Medical Oncology, Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA; [6] Thomas Jefferson University Hospital, Philadelphia, PA*

Introduction: The optimal management of catheter-related thrombosis (CRT) in patients undergoing autologous stem-cell transplantation (ASCT) remains poorly defined. We reviewed the management of catheter-related thrombosis in ASCT patients in our transplant unit over an 8-year period.

Methods: We reviewed all patients undergoing ASCT at Thomas Jefferson University from 2006-2013. Patients with previous history of venous thrombosis receiving anticoagulation at ASCT were excluded. Patients with CRT were identified and management was reviewed. Three populations were identified: No CRT, CRT no anticoagulation, and CRT on anticoagulation. We performed a Wilcoxon Ranks Sum analysis to evaluate blood and platelet utilization in the three groups. We also reviewed major bleeding events (MBE) and secondary thrombotic events (pulmonary embolism, PE).

Results: We identified 214 patients as described in Table 1. The incidence of CRT for the whole group was 11.2%. Of the 24 patients with CRT, 46% were treated with AC and the remaining was observed without AC. The median number of pooled platelets transfused was 14 in the CRT + AC group, 4 in the no CRT and 4 CRT with no anticoagulation groups (p=0.02). The median number of PRBC transfusions in the no CRT, CRT + AC, and CRT with no AC groups was, 2, 4, and 2, respectively (p=0.01). None of the patients with CRT developed a second thrombotic event (PE). Incidence of major bleeding within the CRT + AC group was 27% while in the CRT and no AC group was 15% (p=NS). One patient expired due to the result of a subarachnoid hemorrhage.

Conclusions: A strategy utilizing AC for CRT in the setting of an autologous transplant results in increased utilization of both platelet and PRBC transfusion and is associated with a trend towards a higher risk of major bleeding. There was no

Table 1
Patient Characteristics

	No CRT	CRT + Anticoagulation	CRT with no anticoagulation
Number of patients	190	11	13
Median age at transplant (year)	58	62	60
Male gender	116	6	10
Ethnicity:			
Caucasian	122	7	12
African	47	2	1
Asian	7	0	0
Hispanic	6	2	0
Other/Unknown	8	0	0
Malignancy:			
Myeloma	132	8	8
Non-Hodgkin's lymphoma	34	2	3
Hodgkin's lymphoma	12	0	0
Primary amyloidosis	3	1	2
CLL	2	0	0
AML	2	0	0
APML	1	0	0
Other	4	0	0
Conditioning:			
Melphalan alone	135	9	10
BEAM	48	2	3
Busulfan/Cyclophosphamide	2	0	0
Cyclophosphamide alone	4	0	0
Unknown	1	0	0
Neutrophil engraftment (in days)	11	12	12
Platelet engraftment (in days)	15	17	17

Table 2
Outcome analysis

	No CRT	CRT + Anticoagulation	CRT with no anticoagulation	p-value
Platelet utilization (Number of pooled platelet units)	4	14	4	0.02
PRBC cell utilization (Number of PRBC transfusions)	2	4	2	0.01

difference in the incidence of PE following CRT in patients treated with or without AC in this small cohort of ASCT patients.

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Combination Antifungal Therapy Experience at an Academic Health System

David R. Ha [1,2], *Nina Haste* [2], *Charles James* [2], *Katherine Medley* [2], *Randy Taplitz* [3]. [1] *Clinical and Administrative Sciences, Keck Graduate Institute School of Pharmacy, Claremont, CA;* [2] *Pharmacy, UC San Diego Healthsystem, San Diego, CA;* [3] *Medicine, University of California, San Diego, La Jolla, CA*

Purpose: Invasive fungal infections are becoming increasingly prevalent, particularly in the immunocompromised population. The development of new antifungal agents with novel mechanisms of action has sparked interest in combination antifungal therapies. This study seeks to characterize combination antifungal use at a large academic health system.

Methods: We conducted a retrospective observational study of adult inpatients with the intent of characterizing combination systemic antifungal utilization between the dates of July 1, 2012 and June 30, 2013. Combination antifungal therapy was defined as administration of two or more target systemic antifungals (liposomal amphotericin B, fluconazole, voriconazole, posaconazole, micafungin or terbinafine) for five or more days.

Results: Twenty nine patients received combination antifungal therapy and 36 unique treatment courses were identified. Ten of the 29 patients (35%) were BMT patients. Pneumonia was the most common disease indication (20/29; 69%). Unknown was the most common organism indication overall (11/29; 38%) and within the BMT patient population (6/10; 60%). Among the 36 unique treatment courses the most common combination therapy by drug class was an azole and an echinocandin (53%; 19/36) followed by a polyene and an azole (31%; 11/36).

Conclusion: A significant proportion of the study population both overall (35%) and among BMT patients (60%) received combination antifungal therapy with no identified infecting fungal organism. There is no data to support such a practice. However, in the setting of severe invasive fungal infections, particularly in immunocompromised hosts, using additional antifungal agents may seem less risk-prone than invasive diagnostics like tissue biopsy. These findings suggest that earlier diagnostic methods including tissue biopsy are warranted to avoid unnecessary use of combination antifungal therapy when no pathogen has been identified.

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Effect of Linezolid Administration on Myeloid Engraftment after Allogeneic Hematopoietic Stem Cell Transplantation

Risa Hashida, *Takehiko Mori, Jun Kato, Sumiko Kohashi, Shinichiro Okamoto. Division of Hematology, Keio University School of Medicine, Tokyo, Japan*

Background: Linezolid is effective against drug-resistant Gram-positive bacteria, and has been widely used for the treatment of various infectious diseases due to such bacteria. Although linezolid has a favorable safety profile, myelosuppression is one of its clinically important toxicities. Myelosuppression due to linezolid has not been systematically evaluated in the setting of hematopoietic stem cell transplantation (HSCT). Therefore, effect of linezolid administration on the myeloid engraftment after allogeneic HSCT was retrospectively evaluated.

Patients and Methods: Patients in whom intravenous or oral linezolid (1200 mg/day) administration was initiated before myeloid engraftment following allogeneic HSCT and continued for 5 days or longer were selected from the institutional database. The patient characteristics, duration of linezolid treatment, and myeloid engraftment were retrospectively evaluated by using the medical records.

Results: Fifteen patients were evaluable and enrolled into the analysis. All patients were male, and median age at transplant was 50 years (range, 21 – 60). Underlying diseases were acute leukemia in 11 patients, myelodysplastic syndrome in 2, and myeloproliferative neoplasm and malignant lymphoma each in 1. All but 1 received myeloablative conditioning. Stem cell sources were bone marrow from related or unrelated donor in 10 patients, cord blood in 3, and peripheral blood stem cell (PBSC) in 2. Linezolid was initiated at a median of 12.5 days after HSCT (range, -3–20), whose median duration of treatment was 14 days (range, 5–20). Although all patients achieved myeloid engraftment (absolute neutrophil exceeding 0.5 x 10^9/L), the median day of engraftment was 22.5 days after HSCT (range, 12–33). Japanese national registry data showed that the median days of myeloid engraftment were 12 days and 14 days after allogeneic PBSCT and BMT, respectively (Nagafuji K, et al. Int J Hematol 2010). In 8 (53%) of 15 patients, myeloid engraftment was achieved later than 21 days after engraftment.

Conclusion: Although myeloid engraftment was achieved, the engraftment was considered delayed in patients who received linezolid early after allogeneic HSCT. Although the number of subjects evaluated was small, these results suggest that linezolid could have a potential to delay neutrophil recovery, and should be carefully used after allogeneic HSCT.

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Posaconazole DR Tablet Serum Concentrations in the Bone Marrow Transplant Population: Association with Prevention or Treatment of Invasive Fungal Infections

Nina Haste [1], *David R. Ha* [1,2], *Katherine Medley* [1], *Charles James* [1], *Randy Taplitz* [3]. [1] *Pharmacy, UC San Diego Healthsystem, San Diego, CA;* [2] *Clinical and Administrative Sciences, Keck Graduate Institute School of Pharmacy, Claremont, CA;* [3] *Medicine, University of California, San Diego, La Jolla, CA*

Background: Posaconazole (PCZ) delayed-release (DR) tablets were FDA approved in late 2013 for prophylaxis of invasive fungal infections (IFI). In 3 clinical studies leading to approval, PCZ DR exhibited significant pharmacokinetic advantages over oral suspension (OS), largely due to improved absorption. Historically, subtherapeutic PCZ OS levels were linked with breakthrough IFI. We aim to evaluate PCZ DR serum levels in the bone marrow transplant (BMT) population and link levels to IFI breakthrough prevention and treatment.

Methods: After approval by Pharmacy and Therapeutics, PCZ levels were routinely obtained in BMT patients ≥18 years old started on PCZ DR. A retrospective chart review was performed between January 1 and June 30, 2014. Baseline demographics, PCZ dose and levels, as well as patient specific factors with the potential to affect levels and development of IFIs were collected.